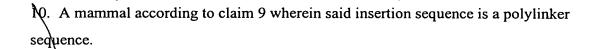
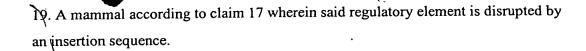
## **CLAIMS**

## We claim:

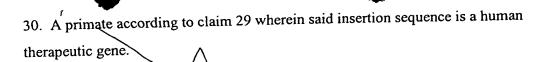
- 1. A non-human manimal comprising a modified endogenous gene, wherein said endogenous gene is selected from the group consisting of a gene or sequence encoding an ion-channel, a G-protein coupled receptor (GPCR), an immunoglobulin, a growth factor, an enzyme, or a milk protein.
  - A mammal according to claim 1 wherein said mammal is a farm animal.
  - 3. A maximal according to claim 2 wherein said farm animal is selected from the group consisting of cattle, sheep, pigs, horses and goats.
- 4. A mammal according to claim 1 wherein said mammal is selected from the group consisting of mice, rats, rabbits, guinea pigs, hamsters and gerbils.
  - 5. A mammal according to claim 1 wherein said milk protein gene is a lactoglobulin gene.
- 6. A mammal according to claim b wherein said lactoglobulin gene is the
  15 α-lactoglobulin gene or the β-lactoglobulin gene.
  - 7. A mammal according to claim 6 wherein said modified  $\alpha$ -lactoglobulin gene or  $\beta$ -lactoglobulin gene does not encode any phenylalanine residues.
  - 8. A mammal according to claim 1 wherein said endogenous gene is disrupted by deletion of at least one nucleotide.
- 9. A mammal according to claim 1 wherein said endogenous gene is disrupted by an insertion sequence.



- 11. A mammal according to claim 9 wherein said insertion sequence is a reporter gene.
- 5 12. A mammal according to claim 11 wherein said reporter gene is selected from the group consisting of a luciferase gene, a β-galactosidase gene and green fluorescent protein (GFP), blue fluorescent protein (BFP), red fluorescent protein (RFP) and yellow fluorescent protein (YFP).
- 13. A mammal according to claim 9 wherein said insertion sequence is selected from the group consisting of a gene encoding human lysozyme, human growth hormone, human serum albumin, human globin, a human immunoglobulin, and a human enzyme.
  - 14. A mammal according to claim 12 wherein said human enzyme is  $\alpha$ -1 antitrypsin.
- 15. A mammal according to claim 12 wherein said human enzyme is anti-thrombin 15. III.
  - 16. A mammal according to claim 12 wherein said human enzyme gene does not encode any phenylalanine residues.
- 17. A mammal according to claim 9 wherein said insertion sequence is selected from the group consisting of a human gene under control of its endogenous promoter, a
  20 modified endogenous regulatory element for an endogenous gene, a transcriptional regulation cassette and a dimerizing sequence.
  - 18. A mammal according to claim 17 wherein said endogenous regulatory element is disrupted by deletion of at least one nucleotide.



- 20. A mammal according to claim 1 wherein said enzyme is a sugar transferase enzyme.
- 5 21. A mammal according to claim 20 wherein said sugar transferase enzyme is α-galactosyl transferase.
  - 22. A mammal according to claim 21 wherein said  $\alpha$ -galactosyl transferase gene is disrupted by deletion of at least one nucleotide.
- 23. A mammal according to claim 21 wherein said α-galactosyl transferase gene is disrupted by an insertion sequence.
  - 24. A mammal according to claim 23 wherein said insertion sequence is a hormone receptor gene.
  - 25. A mammal according to claim 23 wherein said insertion sequence is a viral receptor gene.
- 26. A mammal according to claim 23 wherein said insertion sequence is a G-protein coupled receptor gene.
  - 27. A primate comprising a modified endogenous gene.
  - 28. A primate according to claim 27 wherein said endogenous gene is disrupted by deletion of at least one nucleotide.
- 20 29. A primate according to claim 27 wherein said endogenous gene is disrupted by an insertion sequence.



31. A primate according to claim 29 wherein said insertion sequence is a human antibody gene.

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